OPEN LICENSE OR PATENTS?
RESPONSIBLE CHOICES WITHIN A DIVERSE ECOSYSTEM

Valencia Biocampus iGEM team

Original watercolor by Paula Villaescusa

"*I really like the idea of connecting the IPR discussion to the notion of Responsible Research and Innovation*"

Dirk Stemerding

"*The cover is great! I enjoyed reading the report, which is well-written. (I particularly like the first sentence.)* "

Jane Calvert

" *I very much like the approach and the report*"

Harald König

"*A very nice and interesting report*"

Simone Arnaldi

"*It reads very interesting and your idea to use a mathematical formula seems intriguing to me*"

Philipp Pfingstag

"*I found it very interesting*"

Arianna Neri

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INTRODUCTION.
SYNTHETIC BIOLOGY –AND iGEM AS A CROSSROAD OF BACKGROUNDS AND JARGONS: THE IP CASE

We did not want the Human Practices section to be a cosmetic addendum to our iGEM project. In The St²OOL, we have performed a critical but constructive analysis of four of the pillars of the competition. Three of them are technical, engineering assumptions (**stability**, **standardization**, **orthogonality**). The fourth leg of our St²OOL is for us at least as important as the other three, and deals with the answer to this difficult question: who owns synthetic constructions?

iGEM is linked to the Registry of Standard Biological Parts, a non-profit organization (as iGEM Foundation itself) archiving and distributing thousands of BioBrick parts for free (http://parts.igem.org/Main_Page). *No patents, no patent licenses, no royalties*. Just Open Access (either free online access or free online access under concrete creative commons licenses' terms and conditions). As stated in their Website, it's "an open community that runs and grows on the Get & Give (& Share) philosophy. Users get parts, samples, data, and tools from the Registry to work on their synthetic biology projects. They will give back to the Registry the new parts they have made, as well as data and experience on new and existing parts". But of course, the world of Biotechnology/SynBio is far more than iGEM and a range of Intellectual Property protection formulas do exist. Is iGEM an island of Free Access in an ocean of patentable SynBio achievements?

We decided to focus on Intellectual Property issues because we think it is timely to deal with the topic in a radically new way. Moreover, we strongly believe that the iGEM competition, with its unique mixture of life scientists, engineers, human scientists, companies, academia, etc., is the perfect workbench for an interdisciplinary approach to Intellectual Property protection. As Jason Kelly (Ginkgo Bioworks) funnily mentioned in Twitter, in a recent discussion with iGEM HQ and with the author of "Biology is Technology", Robert Carlson, iGEM is "The Woodstock of SynBio". In the frame of the iGEM competition, the perfect crossroad for this study, we have deliberately dealt with the Human Practices section with the same rigour that we try to use with the other technical issues of The St²OOL Project, our final goal being to bridge the gap between the heterogeneous "tribes" of iGEMites and the complex Intellectual Property scenario affecting SynBio. As the first step of this approach, and in order to create a common language in which we all feel comfortable, we have created a short dictionary of legal terms for scientists/engineers and a twin dictionary of SynBio technical terms for lawyers and Human scientists (see **Annex II**).

INTELLECTUAL PROPERTY (IP). HISTORY AND TYPES[1]

Different forms of Intellectual property in Synthetic Biology:

The IP of the biotechnology companies' businesses displays different forms of protection of vaccines, seeds, plants, strains, medical devices, software, etc. Most of these different assets may attract more than one form of IP protection. In the biotechnology sector, the most relevant forms of IP are patents, although other forms are also applicable and used in practice, namely: utility models, industrial designs, trademarks, trade secrets and copyright, among others.

Table 1 below summarizes some different forms of IP protection that can be used to protect biotechnological inventions[2].

TABLE 1. Different types of IP protection in biotechnological industry

Patents *Isolated polynucleic acids, peptides and polypeptides, enzymes, microorganisms, viruses, vectors, antibodies, probes, vaccines, compositions, expression systems, cell lines, plants, seeds, transgenic organisms, methods for preparation or use of the above.* *Medical devices.*
Trade marks *Words/name, computer icons, graphical designs, multimedia elements or use of the above.* *Medical devices.*
Registered designs *Medical devices, biochemical, biophysical or bio-electrochemical apparatus.*
Trade Secret/Know-how *Laboratory notebooks, design workbooks, customer information, documented internal processes, "data exclusivity" on clinical data generated for therapeutic approval.*

[1] Fact Sheet. Intellectual Property in Biotechnology. European IPR Helpdesk (2014)
[2] Table 1 has been elaborated based on the Spruson & Ferguson Biotechnology Intellectual Property management manual. (2008) 8-28

Plant breeders' or plant variety protection rights

Plant varieties, propagating and harvesting material from plant varieties.

Domain names

Web addresses.

Table 2[3] below details the most common IP tools used on protecting inventions.

TABLE 2. Most common IP tools or IP rights (IPRs)

Patent

It is a legal document, through which a right is granted for an invention, a product or a process that provides a new way of doing something or offers a new technical solution to a problem. A patent provides exclusive rights for a fixed period of time in exchange for public disclosure of the invention. A patent enables the patent owner/holder to exclude unauthorised third parties from making, using, selling, offering for sale or importing for those purposes a product, a process, or a product obtained by a patented process for the term of the patent. It is also the most expensive form of protection and it is regionally restricted (e.g. US patent)

Utility Model[4]

It is an exclusive right granted for an invention with the same function as patents. In fact, they are referred to as "petty patents" or "innovation patents". The main differences between these IP rights are the term of protection, which is less in utility models (UM); requirements for acquiring the right, which are less strict in the UM; the acquisition and maintenance fees, which are generally lower in UM; and the fact that UM may only be obtained for certain fields of technology and only for products but not for processes or methods. A particular feature of this right is that it does not exist as a possible legal form of IP protection in every country[5].

[3] Fact Sheet. Intellectual Property in Biotechnology. European IPR Helpdesk (2014), 4
[4] http://www.wipo.int/sme/en/ip_business/utility_models/utility_models.htm
[5] According to WIPO, countries and regions that provide utility model protection are: Albania, Angola, Argentina, ARIPO, Armenia, Aruba, Australia, Austria, Azerbaijan, Belarus, Belize, Brazil, Bolivia, Bulgaria, Chile, China (including Hong Kong and Macau), Colombia, Costa Rica, Czech Republic, Denmark, Ecuador, Egypt, Estonia, Ethiopia, Finland, France, Georgia, Germany, Greece, Guatemala, Honduras, Hungary, Indonesia, Ireland, Italy, Japan, Kazakhstan, Kuwait, Kyrgyzstan, Laos, Malaysia, Mexico, OAPI, Peru, Philippines, Poland, Portugal, Republic of Korea, Republic of Moldova, Russian Federation, Slovakia, Spain, Taiwan, Tajikistan, Trinidad & Tobago, Turkey, Ukraine, Uruguay and Uzbekistan

Trade Mark

It is a distinctive sign that identifies certain goods and/or services of a (natural or legal) person from those goods and/or services owned or provided, respectively, by another (natural or legal) specific person. Trade marks may be obtained for the brand name of a particular product or process.

Copyright and Related Rights

Provide the right to the author(s) to use its own creative works – including but not limited to artistic works, literary works, software and databases – but do not cover ideas, procedures, operation methods or mathematical concepts as such.

Registered Design Right

Is an industrial property right granted by its owner, that protects the visual design of an item. The industrial design protection takes into account the aspect and aesthetic of the device in any field and, in particular, in Life Sciences and in the biotechnology field.

Domain Name

Is the relevant address of a Website. It consists of one or more parts that are conventionally concatenated, and delimited by dots, such as "something.com". Domain names may refer to an existing product or mark; however they are susceptible to be requested by the holder of an identical or similar (to the registered domain name) prior trade mark in case there exist two different owners.

Plant Breeder's Rights / Plant variety protection rights

Are rights granted to the breeder of a new variety of plant which is distinct, uniform and stable. They provide the breeder with the exclusive control over the propagating material (i.e. seed, cuttings, divisions, tissue culture) and harvested material (i.e. cut flowers, fruit, foliage) of a new variety for a concrete number of years.

Trade Secret and Know-How

Are valuable forms of IP. The term "know-how and "trade secrets" are a subset of confidential information in the context of business, commerce or trade. Trade secrets are valuable as long as they are kept secret, which can be done, for instance, through confidentiality or non-disclosure agreements. In fact, trade secrets and know-How exist provided that (i) no disclosure of the secret / know-how is made and (ii) the owner of this secret / know-how does all its efforts to keep the secret / know-how confidential, including the implementation of protective measures.

The choice of a particular IPR will depend on different factors such as the inventor's area of specialization, the structure of the invention, anticipated activities and commercial application among others. Related to the actor's area of specialization, she/he should think about which is the best option to protect her/his invention. On the structure of the invention, it is important to analyse how one's invention is structured and which are its characteristics. As an example, imagine an invention which could be protected with both patents and utility models; one should check which structure better matches the invention's structure depending on whether the invention is a product, process or method, whether this invention meets patentable standards, etc. On anticipated activities, this refers to which activities are expected to be conducted as an application of the invention.

Patents in Synthetic Biology:

As in other technological fields, SynBio/ biotechnology patents are used to protect inventions that provide a solution to a technical problem, including the way they work or how they are used. They grant their owners the exclusive right to prevent others from making, using, selling, offering for sale, or importing an invention without their consent, on a defined territory, for a limited period of time[6].

The rationale behind the patent protection for biotechnology inventions is related to the fact that:

- Patents give the possibility to the inventor to recoup the investment done in the obtaining of a new biotech product or process.
- Patents require the disclosure of the new technology subject to the invention for the benefit of society. Disclosing the new technology to the public inspires further research, development and innovation. Unfortunately, the public cannot use or exploit this new technology until the end of the exclusive period conferred by the patent since its application date. Thus patents are a very rich source of technical information.

Like other patents, biotechnology patents also contain:

- A description of the invention itself with specific details and the advantages that this invention brings in comparison with the prior art or the state-of the art, and examples;
- A set of claims, which define the subject for which protection is sought.

[6] In Europe or in the USA, the protection lasts twenty years from the first filing of the patent application.

In biotechnology, claims are mostly related to:

- Product claims
- Use claims
- Method of production claims

What characterizes biotechnology patents is that they are defined as patents belonging to a defined list of Patent Classification codes.

In general, to be patentable, biotechnological inventions need to meet the same requirements as inventions in other technology fields.

BIOLOGICAL METAPHORS AND IP: THE DIVERSE ECOLOGY SCENARIO

One of the reasons why we chose to study IP issues was the appealing metaphor of the ecological diversity of protection forms. The main work we have analysed for the present report is a Jane Calvert's article published in 2012 and entitled "Ownership and sharing in synthetic biology: a 'diverse ecology' of the open and the proprietary?". In discussion with other members of the Valencia Biocampus team, Paula got interested in the concept and prepared the watercolor that illustrates this report. When we proudly sent a preliminary version of the present report to Jane Calvert, and along with several suggestions and comments, she kindly stressed: "*I should say that the 'diverse ecology' idea is not mine – it comes (like many things in synthetic biology) from Drew Endy*." Indeed, in an online pdf document (available under a Creative Commons Attribution 3.0 US License here: http://openwetware.org/images/f/fd/Why_the_BPAv1.pdf), Endy describes the importance of Property Rights for biotechnology and Synthetic Biology, with examples such as the well-known case of artemisinin, and highlights the contrast with patent-free issues such as, yes, the iGEM competition (*Connection or Collision?* he wonders). And then on the 11th slide, the magical term appears: "*Our Combined Opportunities: (…) Enable a rich, fully* ***diverse ecology*** *of commercial and public benefit use from the outset*". One of the solutions of this ecological puzzle is The BioBrick Public Agreement (BPA), which combines freedom of use with –theoretically- patent compatibility. When a researcher contributes a part under the BPA, others, who have also agreed to the BPA User Agreement can freely use that parts (and one can use their parts as well). In summary, Drew Endy recognized the problem of IP in SynBio and proposed BPA as a compromise solution between two views in conflict.

Back to J. Calvert's work, she also described, and in great detail, the two approaches in conflict, using John Craig Venter Institute as a flagship example of gene patent-oriented research in Synthetic Biology; and parts-based approaches –among them, again, iGEM-, as an example of engineering-inspired open "bio-software". Maybe in the search of a common ground, she stressed the shared metaphors used by practitioners of the two approaches, both of which, she thinks, "*have a place in a vision for the future of synthetic biology as a 'diverse ecology' of the open and the proprietary*". In fact, it could be that the technical and historical framework of each of the approaches is shaping their view regarding Property Rights, with biotechnology-inspired chemical synthesis of genomes naturally expecting protection trough patents, and engineering-inspired *iGEMers* displaying an Open License-friendly attitude.

The evolution of SynBio is uncertain, which does not mean that it will not have a bright future, but that *which* future it will be is difficult to be predicted now. Similarly, it is not possible to forecast the evolution of the protection landscape, as it is linked with the technological development of the discipline, its interactions with the market, and conceptual tensions among its practitioners. Time will what say the evolutionary fate of this legal ecosystem will be, which can be impoverished down to simply two approaches in conflict or *flourish*, in Calverts' words, as a myriad of intermediate forms.

RESPONSIBLE RESEARCH AND INNOVATION: IMPLICATIONS FOR IP

Responsible Research and Innovation (RRI) is a term that has increased its relevance during the last two years, in particular within the European Commission's Science in Society program, in the context of the Horizon 2020 Strategy[7]. The term RRI started to appear in the first decade of the 21st century in the academic and policy literature due to a re-framing of 'Science *in* Society' to 'Science *for* Society, *with* Society' and, the directing of science and innovation towards societal 'grand challenges' Europe was (is) facing. However, until 2011 it lacked conceptual weight, which appeared thanks to the RRI definition proposed by Von Schomeberg (shown below)[8]. There are different examples where RRI could be used in a science discipline, from climate impact of a research to legal, social and ethical implication of it. In this part, we have tried to understand what this *"trending topic*" is and why it is important in our issue; because science and engineering is not only about creating new inventions, we should do it in a manner where broader aspects above the pure laboratory work are taken into account[9]. Society players should work together during research and innovation process in order to better align both the process and its outcomes with the values, needs and expectations for our society[10].

> *"A transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society)"*[11].

Regarding SynBio and its interaction with RRI, we want to stress Conor M.W. Douglas and Dirk Stemerding's work about ruling SynBio for recovering new health frontiers[12]. We consider this report as one of the main references in the field as we pointed out in our previous Human Practices project during iGEM 2013 competition. In fact, in the last edition of iGEM, we focused on studying the meaning of RRI and how iGEM could help SynBio to match **RRI principles**: **engagement**, **gender equity**, **science education**, **transparency**, **ethics** and **governance**. In order to do that we recorded a laboratory diary in which not only magnificent results were shown, but we also described our not achieved goals, failures and mistakes. Also, we brought up to date the dry and wetlab work in the notebook wiki page in order to keep everyone informed and let anyone interested follow our project, step by step. Moreover, we completed the iGEM 2013 Basic Safety Form and submitted it to the iGEM European Biosafety Committee, a survey to find out how research topics are chosen by professional researcher, and we made a book called "Ten tales on Synthetic Biology", where five of us gave a negative and catastrophic point of view of how the world could become if SynBio would be used maliciously;

[7] European Commission. Communication from the commission to the European parliament, the council, the European economic and social committee and the committee of the regions. Horizon 2020 - The Framework Programme for Research and Innovation. (2011)
[8] Stilgoe, J. Developing a framework for responsible innovation. Research Policy (2013) **42** (9), 1568-1580
Owen, R., Macnaghten, P., Stilgoe, J. Responsible research and innovation: From science in society to science for society, with society. Science and Public Policy (2012) **39** (6), 751-760
[9] C. Douglas & D. Stemerding. Challenges for the European governance of synthetic biology for human health. Life Sciences, Society and Policy (2014)
[10] Valencia Biocampus report. RRiGEM: Responsible Research and innovation and how it affects iGEM. (2013)
[11] M. Grace & B. Stahl. Responsible Research and Innovation. Critical reflection into the potential social consequences of ICT. IEEE Code of Ethics (2013)
[12] C. Douglas & D. Stemerding. Governing synthetic biology for global health through responsible research and innovation. Springer Science (2013)

whereas the remaining five were assigned an optimistic point of view. This time, our goal is to focus on **RRI** to make it the **centre of the IP decision process**.

Our project for iGEM 2013 dealt on how RRI could be used in SynBio throughout iGEM competition values. This year we have worked as well the idea of RRI, but from an IP perspective. This idea arose from the above mentioned Conor M.W. Douglas and Dirk Stemerding work about RRI in SynBio. They stressed that SynBio is characterized by its potential "usability"; nevertheless, it does not supplant classical techniques for preventing and treating illnesses and it can be best understood as a supporting framework of tools and techniques that can offer potentially outstanding contributions[13]. For example, SynBio can be used to develop a new version of the antimalarial compound artemisinin, such as the famous achievement by Jay Keasling's lab[14]. It can also turn out to be a successful approach to develop novel and low-cost diagnostics and biosensors by engineering biological systems; it can develop new biofuels; it can be applied to produce and deliver antigens as oral ingested vaccines; or it can pave the way towards an innovative strategy to engineer safer, stronger and more nutritious crops, among other things[15].

We want to boost SynBio in an IP frame, which means seeking for 'the right impact', as Douglas and Stemerding would say. We believe we should be able to choose the right way to keep a balance between the opposite forces from different players such as ownership and sharing views.

[13] C. Douglas, D. Stemerding. Governing synthetic biology for global health through responsible research and innovation. Springer Science (2013)
[14] Hollis A. Synthetic Biology: ensuring the greatest global value. Systems in Synthetic Biology. Doi: 10.1007/s11693-013-9115-5 (2013).
[15] C. Douglas, D. Stemerding. Governing synthetic biology for global health through responsible research and innovation. Springer Science (2013)

OUR PROPOSAL: RRI AS A TOOL TO CHOOSE WITHIN THE IP ECOSYSTEM

The more we studied **RRI**, the more we liked it. Not unlike scientific research, RRI is about common sense, about combining self-profit with others' profit, about taking care of our planet. We believe that being responsible is not the opposite of being selfish; responsibility is just a broad-minded way of selfishness that points at the long-term benefit. And there is no long-term benefit without a sustainable society in a sustainable environment. What is good for our neighbours and for our home must be good for us as well.

Since we, our Human Practices sub-team, are a biotechnology and a law student, we are also glad to see that another key concept in IP is a beautiful science-law metaphor: Jane Calvert & Drew Endy's **"diverse ecology" scenario**. This image fits well with our interdisciplinary spirit and we found it very useful because it evokes very elegantly the range of different solutions out there to choose from in order to use a scientific invention in a given way.

Having reached this point, it is obvious which the next step is: there is a whole ecosystem of IP figures (see the poetic cover illustration by Paula, another team member), and one has to be chosen. How? Our bet is simple: by using RRI principles (**mutual learning**, **human resources management**, **fundamental rights respect**, **reseach formation** and **transparency**) as the main guide the decision process.

The following figure illustrates what we propose:

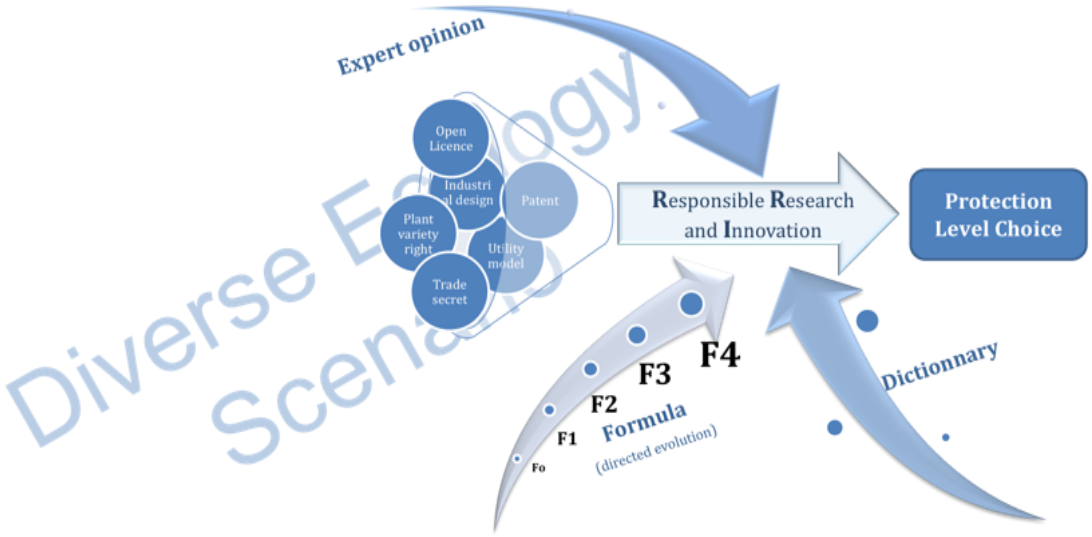

Figure 1. RRI-based decision process on a diverse ecology scenario. From a diverse array of IP protection possibilities (diverse ecology scenario), we propose RRI as a framework to choose the most suitable one. In order to assist in the decision process, experts' opinion is the major force, and we propose here two tools to contribute to this process: a formula-based assistance procedure (**Annex I**) and a common language exemplified by our dictionaries (**Annex II**).

In our view, the decision process has to fall upon the responsibility of the experts or examiners, as it is the case today. But we propose that a formation on RRI for patent examiners and other IP actors, as stakeholders, is introduced. In the same way that scientists need a basic law background for transferring their knowledge into applied solutions, we envisage a future in which everybody involved in the production of a given IP figure (a patent, for example, from scientists and engineers to ethics specialists, lawyers and other experts) should share a common interdisciplinary formation on RRI. A common language is the first step towards a common goal.

Additionally, we propose in this report **two tools** that might contribute to avoid misunderstandings and to make a simplified decision process available for a wide audience. In order to accomplish the former objective, we have prepared the **two common-languages short dictionaries** listed in **Annex II**. To achieve the latter, we propose, for the first time for the best of our knowledge, **a math-based equation** that could contribute to make IP issues available to a wide audience (for a complete description, see **Annex I**). We have prepared the equation in two steps. First, we combined the patentability requirements (novelty, inventive step, industrial application) in a mathematically logical way to reach our draft equation (**Fo**, **Annex IA**). Then, we submitted the formula to several experts to have their feedback, and thus modify **Fo** accordingly to yield **F1** (this reflexive process, combining design with improvement rounds, elegantly evokes a biotechnology strategy called directed evolution, see **Annex IB**).

A) $\mathbf{P.I.} = \mathbf{M} \times \mathbf{N} \times (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$ Expert1 Expert2 Expert3 $\mathbf{P.I.} = \mathbf{R} \times \mathbf{N} \times (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$

B)

C)

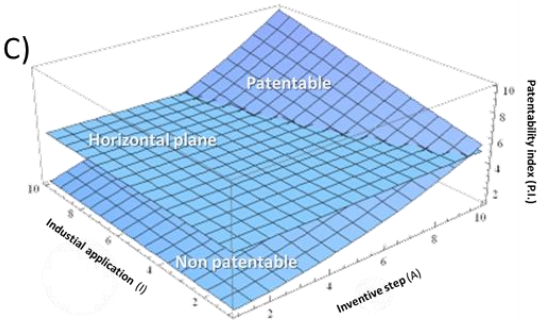

Figure 2. Human decisions are only acceptable if no help is used? **A)** Directed evolution of the formula (**P.I.**: Patentability Index (0-10), **M**: Morality (0/1), **N**: Novelty (0/1), **A**: Inventive Step (1-10), **I**: Industrial Application (1-10), **R**: Responsibility(0-1)). **B)** Chess player. **C)** Graphic representation of the equation **Fo** we initially proposed for patentability determination, as a function of the Industrial application (**I**) and the Inventive step (**A**). See **Annex I** for details.

The very idea of using maths to decide whether something is patentable may seem odd. The opinion of the law experts was useful; but we wanted to have a broader feedback from other social actors. We thus carried out a survey to probe the opinion of *iGEMers*, scientists/engineers and law students, but also of ordinary people to compare their view on our proposal. The **C section** of **Annex I** describes the results of this survey that can be summarize as follows: the vast

majority of the 526 respondents (70 to around 80%) found that a math-based approach could be a useful tool, but should not substitute humans as the final decision makers. We could not agree more on that.

ANNEX I.
OUR PATENTABILITY INDEX

There are many elements the protection of which, in legal terms, is desirable (see the orange box below). However, not all of them are susceptible to patent, but a small group (in white) that must also have some characterictics, namely: **Novelty**, **Inventive Step** and **Industrial Application**.

An idea – Scientific Theories – Mathematical Methods – Art Creations – Commercial or Economical Activities – Computer Programs or Software – Objects (Products...)* – Presenting Information Methods – Vegetable or Animal Varieties – Images – Designs – Words or Sentences – Signs – Plays (Artistic, Literary, Scientific) – Procedures or Manufacturing Methods

*If it only provides an improvement to an existing product: Utility Model

Table 1. *Different human creations are shown. In white, see human-made things/discoveries that could be patented. In orange, the ones that in case of being protected would need other kind of legal (non-patent protection).*

Traditionally, experts decide whether something is patentable or not. In an effort to assist those experts, we, the Valencia Biocampus iGEM team, describe below an intuitive formula that might be helpful for them and also for other actors in SynBio (e.g. engineers, scientists, DIY biologists) when it comes time to take a decision. The formula we propose is based in internationally accepted standards and articles related to the topic (see bibliography and references).

A. THE FORMULA. F_0

Extended F_0 ecuation

$$\text{Patentability Index } [\mathbf{P.I.}] = \text{ Morality } (\mathbf{M}) \text{ x Novelty } [\mathbf{N}] \text{ x (Inventive Step } [\mathbf{A}])^{\log\left(\frac{\text{Inventive Step [A]+ Industrial application [I]}}{2}\right)}$$

Please note that we introduce in the formula a non-legal term, morality.[16]

Abreviatted F_0 ecuation

$$\mathbf{P.I.} = \mathbf{M} \text{ x } \mathbf{N} \text{ x } (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$$

[16] In Europe, the terms of morality & ordre public are mentioned in European patent Convention.

The numerical limits of the formula and the mathematical interpretation (modelling) of the P.I. value are shown at the end of Annex IA.

How does the formula work?

By answering specific question the values of the different parameters in the equation can be introduced.

Previous questions (If any of the answers is "Yes" the invention could not be patented):

- Is your invention about or related to the following fields…

- scientific theories and mathematical methods?	Yes	No
- artistic/literary creations?	Yes	No
- aesthetic creations?	Yes	No
- schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers?	Yes	No
- methods for presenting information.	Yes	No

Breakdown of terms

- **Morality (M). Values: 0/1**

The value of **M** is not arbitrary, but a result of a questionnaire. If any of the answers is "Yes", the term of morality (**M**) automatically becomes zero.

- This invention relates to…

- isolated genes?*	Yes	No
- sequenced DNA?*	Yes	No
- medical procedures?	Yes	No
- embryonic stem cells?	Yes	No
- methods of chromosome transfer?	Yes	No
- mixing of human and animal species?	Yes	No

- Could this invention result in…

- denigration or human dignity?**	Yes	No
- destruction of human life?	Yes	No
- ownership of human life?	Yes	No
- spread of pollution or disease?	Yes	No
- loss of genetic diversity?	Yes	No

If the aim is to protect the DNA* per se*, it must be noted that patent eligible subject matter is "anything under the sun made by humans". The relevant point here is not if the creation is a living or an inanimate thing, but if they are* ***products of nature**, whether living or nor, or* ***human made inventions****.*

To sum up: *DNA per se. Not patentable.* ✖

Applications arose from the presence/use of that sequence. Patentable. ✔

*** Given the high diversity of the use of dignity throughout the judicial world, human dignity could be understood as a set of three minimum elements: an ontological, a relational and a limited-state claims. The ontological one refers to "the inherent dignity of man"; the relational claim relates to the intrinsic worth and the recognition respect of it by others; finally the third claim recognizes the intrinsic worth of individual in such a way that the state should exist for the sake of the individual human being, and not* viceversa.

- **Novelty (**N**). Values: 0/1.**

Similarly, **N** is calculated from the answers to several questions. If any of the answers is "Yes", the term of novelty automatically becomes zero.

Is there a process or product identical to yours (prior state of art)?*	Yes	No
Has the invention been used in public so its operation made is known?	Yes	No
Have the details of the invention publicly disseminated?**	Yes	No

**For answering this question, one has to perform an online search, using the invention/creation keywords, in the following browsers/databases:*

European Patent Office (EPO) *Spanish Patent & Trademark Office (OEPM)*

United States Patent and Trademark Office (USPTO) *Japan Patent Office (JPO)*

PubMed Database *SCOPUS Database*

An invention shall be taken to be new if it does not form part of the state of the art.

The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else) which has at any time before the priority date of that invention been made available to the

public (whether in the country where the invention would be patented or elsewhere) by written or oral description, by use or in any other way.

***The discussion of the details related to the invention with fellow researchers, partners and advisors is considered as confidential. It is highly recommended to sign confidential agreements.*

- **Inventive Step (A). Values: 1-10.**

By contrast with **M** and **N**, inventive step (**A**) may be any value between 1 and 10. This test has an initial value of 1 and 3 points for each of the options/answers bold marked can be added up a total **A** value of 10.

If the invention/creation is the combination of several ones, are their properties or functionality predictable if you know all its components? *	Yes	**No**
If the invention/process is the solution to a problem, are there different solutions possible so the inventor had to research and select the best one?**	**Yes**	No
Is the invention the replacement of one of the components of the product/process for a different one with equivalent properties?	Yes	**No**

**If the properties are greater than the sum of its parts, or better than expected, then it can be considered as a non-obvious invention. And then, the answer to the previous question should be "No".*

Summing up: patentability requires that several features are met (including: surprising technical advantages, unexpected technical effects). Mere aggregations (developments in one way street -lack of alternatives) are not patentable.

***If there is only one solution to a problem in a process, object or invention, and it could be deduced by a person skilled in the art, it might be considered obvious.*

- **Industrial Application (I). Values: 1-10**

This test has an initial value of 1, to which are added 3 points for each of the options/answers bold marked.

Is the industrial field totally clear in the invention description?*	**Yes**	No
Is the main application of the invention related to the private and personal sphere of human being?	Yes	**No**
Is the invention described clear and complete enough for being carried out by a person skilled in		

	the art?**	**Yes**	No
✚	Is the invention a method for treatment of the human or animal by surgery or therapy or a diagnostic method practiced on the human or animal body?***	Yes	**No**

**It must be specified the industry the invention is addressed to (the term "Industry" is far-reading). It is especially important when the invention refers to DNA sequences.*

An invention shall be taken to be capable of industrial application if it can be made or used in any kind of industry, including agriculture.

***Requirement of sufficiency of disclosure.*

Disclosure*: the matter relied upon as prior art must disclose subject matter that, if performed, would necessarily result in an infringement of the patent.*

*******Eliminatory question****. If the answer to this question is "Yes" the P.I. automatically becomes "0". This restriction does not apply to an invention consisting of a substance or composition for use in any such method.*

Limits and mathematical interpretation (modelling of F_0)

As we mentioned above, our HP team has developed an equation for the field of intellectual property, based in the current laws on this issue.

$$P = M \cdot N \cdot \left(\frac{A+I}{2}\right)^{\log(A)} \quad (1)$$

Where:

$P \in \{0,1,\dots,9,10\}$ is patentability.

$M \in \{0,1\}$ is morality.

$N \in \{0,1\}$ is novelty.

$A \in \{1,2,\dots,9,10\}$ is inventive step.

$I \in \{1,2,\dots,9,10\}$ is industrial application.

Both morality and novelty are strict criteria with only two possible values: they must be one in order to be patentable and they are the main barriers in patentability. Once they are overcome, patentability becomes more ¿subjective? This term is the most interesting, in a mathematical way, to analyse. So we can define:

$$P_c = \left(\frac{A+I}{2}\right)^{\log(A)} \quad (2.a)$$

or

$$P_c = A^{\log\left(\frac{A+I}{2}\right)} \quad (2.b)$$

Proof:

$$P_c = \left(\frac{A+I}{2}\right)^{\log(A)} \rightarrow \log(P_c) = \log\left(\left(\frac{A+I}{2}\right)^{log(A)}\right) \rightarrow \log(P_c) = log(A) \cdot log\left(\frac{A+I}{2}\right) \rightarrow$$

$$\rightarrow \log(P_c) = \log\left(A^{log\left(\frac{A+I}{2}\right)}\right) \rightarrow P_c = A^{\log\left(\frac{A+I}{2}\right)}$$

Using 2.b equation, A variable is more important than I. Independently of any value of I, patentability is always one when A takes the value of one.

The other extreme situation takes places when A is maximal: The patentability increases linearly with the Industrial application.

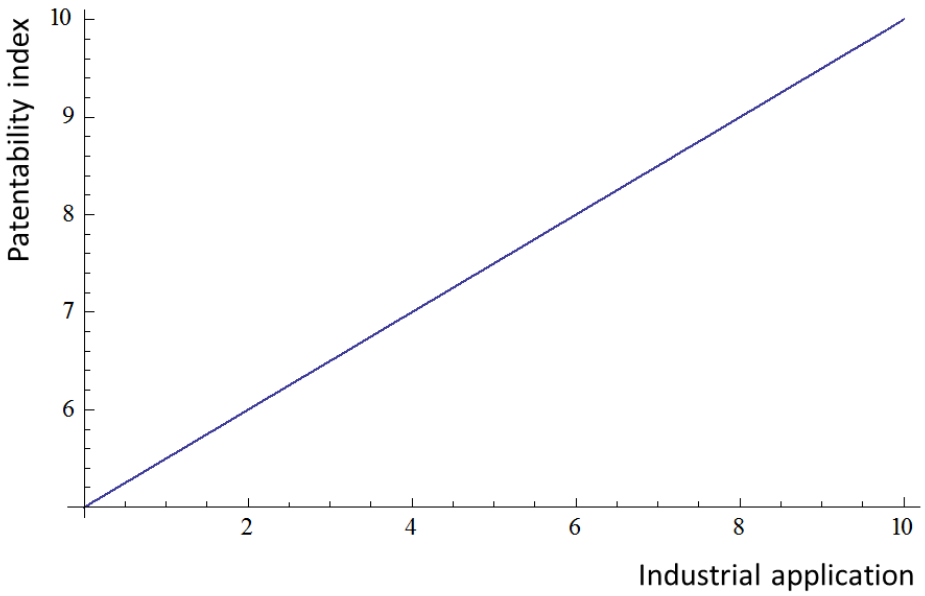

Figure 3. At a maximal value of **A**, the Patentability Index (**P.I.**) value increases in a linear way as industrial application as the Industrial application (**I**) does.

Figure 4 shows three plots depicting the patentability as function of the **Industrial application** (I) and the **Inventive step** (A) -the terms of **Morality** (M) and **Novelty** (N) must be necessarily one; if not, the final value of the **Patentability Index** (P.I.) would be zero and there would be no need to A and I values.

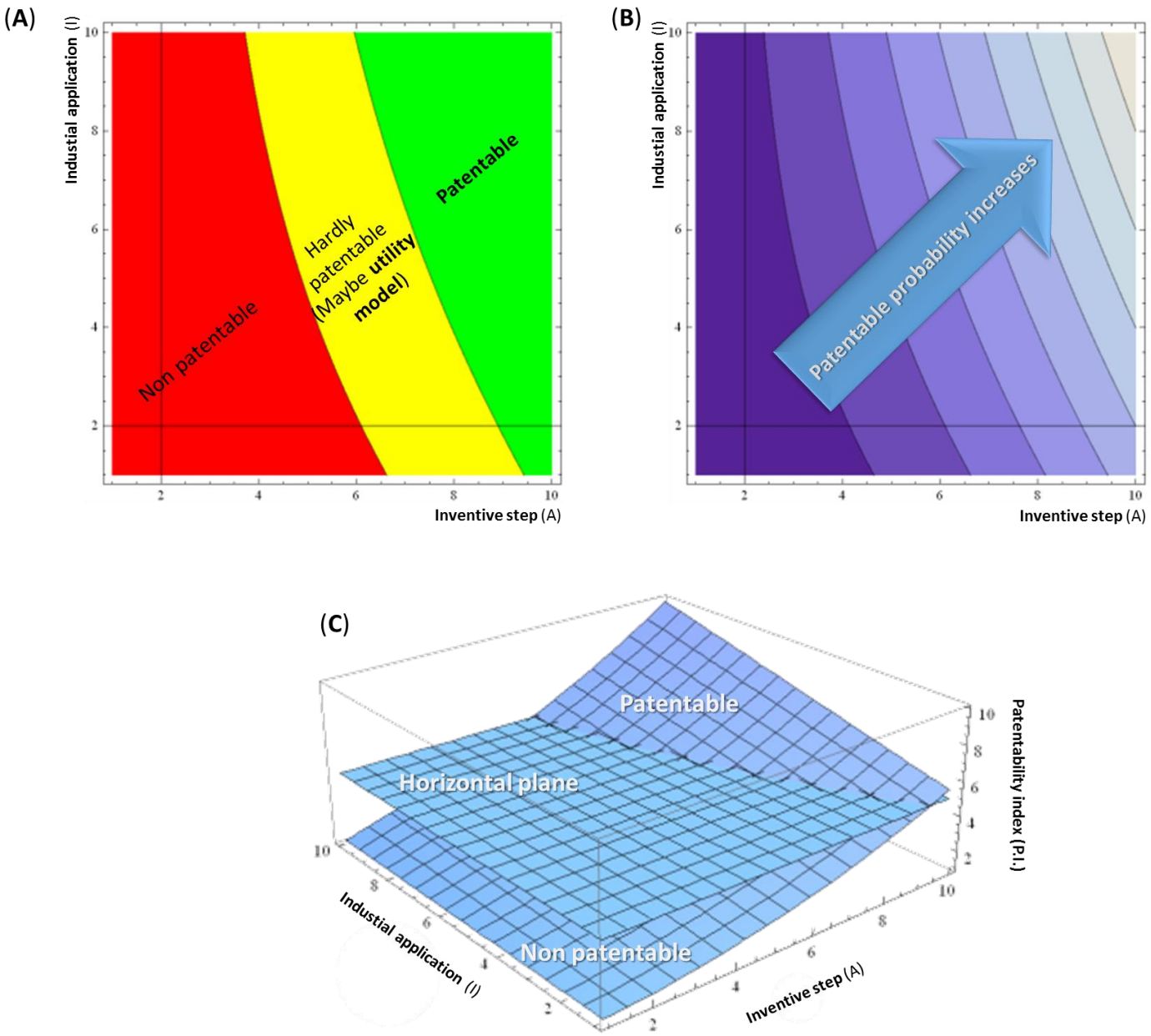

Figure 4. A, main regions of patentability: no patentability in red, hardly patentable in yellow (in this case the inventor should consider protecting by utility model when allowed in the particular country or improving the invention in order to rise it to a stronger position in terms of patentability), and total patentability in green. **B**, proportional regions depending of the different values taken by the A & I parameters (note that the index final value strongly relies on A rather than on I). And finally, the third plot (**C**) shows the graphical representation of the formula in three dimensions with the separation at threshold of 5. The horizontal plane sets the limit of patentability.

B. DIRECTED EVOLUTION OF THE FORMULA (Experts' comments and suggestions)

In this subpart of the **Annex I,** the comments and suggestions from the experts we sent the draft of the report to, are shown. We wanted this process to be like an article review in which we considered those comments as minor/major revisions to build our definitive version of the formula.

Experts' comments and suggestions

Expert1:

"Should the formula (and its criteria / questions) be applicable internationally, i.e. beyond Europe? (e.g. regarding Morality (M) in the formula: US patent law does not (explicitly) require that inventions meet "moral standards", while the 'European Directive on Legal Protection of Biotechnological Inventions' does (and prohibits inventions that offend the "order public" / public morality)."

"Some sentences/explanations on what resources the user of the formula should refer to in order to answer human dignity questions (presumably you refer to case law or present/past judgments on similar/related patent claims; in any case, the approach might specified) could be included."

"Decisions to file a patent claim are dependent on many interests/conditions and two different persons can take opposite decisions on the basis of the same information. This contextual interpretation might be stressed at some point (and it seems in line with your view that the formula does not replace "human decisions")."

Expert2:

"It would be appropriate to mention the TRIPS Agreement and the European Directive 98/44 on the legal protection of biotechnological inventions."

"The legal rules make reference to "ordre public and morality". The legal concepts are not exactly the same. If you want to summarize this concept with the expression "morality" it would be appropriate to specify and explain this."

"The analysis of the cases Diamond v. Chakrabarty, Association forMolecular Pathology et al. v. Myriad Genetics, (US cases) and Monsanto Technology LLC contra Cefetra BV e altri (C-428/08) (UE Court of Justice) would be highly recommended." (Related to the morality test)

"In Association for Molecular Pathology et al. v. Myriad Genetics you will find that not necessarily a genetic sequence used for industrial reasons shall be patented [...], the difficulty in these kind of situation is not necessarily based on morality, but on the inventive step."

Expert3:

“Is morality really a completely "non-legal term"?”

Expert4:

“In your notes it might be worth pointing out that non-natural (synthetic) DNA sequences are patentable.”

“Even if something can be patented (even if it fulfils both the moral and the technical criteria for patentability), then there may still be reasons that someone might decide not to go ahead and patent. One reason might be to avoid ‘patent thickets’ or ‘blocking patents’, where there are so many patents that this inhibits the progress of research. Heller and Eisenberg’s paper, is a classic reference here. I think one of the motivations behind openness in synthetic biology is related to this. It is to attempt to stop people patenting the parts, which would make it very hard to claim IP on a device or system that used a combination of many different parts.”

“After you have had the final results of your survey, it would be interesting if you could reflect on these results, and discuss what they mean for your formula.”

Expert5:

“How exactly RRI fits in the discussion and formula you present in the rest of the report, including Annex II? In the formula you faithfully try to represent the internationally accepted standards relating to IPR. RRI could also be used in this context as a framework which extends the set of internationally accepted standards to include broader societal and ethical considerations in deciding whether you would like to patent a particular achievement. So, instead of the M (morality) you could include an R (responsibility) in your formula, whereby I would prefer to scale the value of R from 0 to 10.”

Annex IC *describes the improved version of the equation we have prepared according to the experts’ comments and suggestions. The main improvements are: the change of the* ***M*** *(morality, possible values: 0/1) term of the initial formula for* ***R*** *(responsibility, possible values: 0-1) and the addition of jurisprudence and articles for clarifying the questions of each formula section.*

C. THE FINAL FORMULA. F_1

Extended F_1 ecuation

$$\text{Patentability Index } [\mathbf{P.I.}] = \text{ Responsibility}(\mathbf{R}) \text{ x Novelty } [\mathbf{N}] \text{ x (Inventive Step } [\mathbf{A}])^{\log\left(\frac{\text{Inventive Step [A]+ Industrial application [I]}}{2}\right)}$$

Please note that we introduce in the formula a non-legal term, responsibility.

Abreviatted F_1 ecuation

$$\mathbf{P.I.} = \mathbf{R} \text{ x } \mathbf{N} \text{ x } (\boldsymbol{A})^{\log\left(\frac{\mathbf{A}+\mathbf{I}}{2}\right)}$$

The numerical limits of the formula and the mathematical interpretation (modelling) of the P.I. value are shown at the end of Annex IA.

How does the formula work?

By answering specific question the values of the different parameters in the equation can be introduced.

Previous questions (If any of the answers is "Yes" the invention could not be patented):

- Is your invention about or related to the following fields...

- scientific theories and mathematical methods?	Yes	No
- artistic/literary creations?	Yes	No
- aesthetic creations?	Yes	No
- schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers?	Yes	No
- methods for presenting information.	Yes	No

Breakdown of terms

- **Responsibility (R). Values: 0-1**

The value of **R** is not arbitrary, but a result of a questionnaire.

If any of the answers for the following questions is "Yes", the term of responsibility (**R**) automatically becomes **zero**.

- This invention relates to...

- isolated genes?*	Yes	No
- sequenced DNA?*	Yes	No
- medical procedures?	Yes	No
- embryonic stem cells?	Yes	No
- methods of chromosome transfer?	Yes	No
- mixing of human and animal species?	Yes	No

- Could this invention result in...

- denigration or human dignity?**	Yes	No
- destruction of human life?	Yes	No
- ownership of human life?	Yes	No
- spread of pollution or disease?	Yes	No
- loss of genetic diversity?	Yes	No

If the aim is to protect the DNA* per se*, it must be noted that patent eligible subject matter is "anything under the sun made by humans". The relevant point here is not if the creation is a living or an inanimate thing, but if they are **products of nature, whether living or nor, or **human made inventions**.*

To sum up: *DNA per se. Not patentable.* ✖

Applications arose from the presence/use of that sequence. Patentable. ✔

*IMPORTANT: **Non-natural** (synthetic) **DNA** sequences **are** patentable ("human made")*

For clarifying this question:

Association for Molecular Pathology et al. v. Myriad Genetics (USA): "merely isolating genes that are found in nature does not make them patentable, but cDNA is patent eligible because it is not naturally occurring".

***Given the high diversity of the use of dignity throughout the judicial world, human dignity could be understood as a set of three minimum elements: an ontological, a relational and a limited-state claims. The ontological one refers to "the inherent dignity of man"; the relational claim relates to the intrinsic worth and the recognition respect of it by others; finally the third claim recognizes the intrinsic worth of individual in such a way that the state should exist for the sake of the individual human being, and not* viceversa.

If any of the answers for the following questions is bold marked **0.3 points** can be added up to a total **R** value of 1.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Heller, M.A. & Eisenberg R.S. Can patents deter innovation? The anticommons in biomedical research. Science (1998) 280 (698), 698-701

May the fact that the invention is protected result in a blockage of the research progress? *	Yes	**No**
Would the patent release some information or advanced useful -in terms of technology or research-, that in case of not being patented would be hidden (by trade secret, for example)?	**Yes**	No
Could the invention result in a solution to an important societal problem?**	Yes	**No**

**If the answer is affirmative, one might decide not to go ahead on patenting considering the possible damage to the growth of knowledge and to the scientific development, even when the moral and the technical criteria for patentability result in a positive Patentability Index value.*

*** If the answer is affirmative, one might decide not to go ahead on patenting considering the welfare that would be restricted to the population, even when the moral and the technical criteria for patentability result in a positive Patentability Index value.*

- **Novelty (**N**). Values: 0/1.**

Similarly, **N** is calculated from the answers to several questions. If any of the answers is "Yes", the term of novelty automatically becomes zero.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Merrell Dow Pharmaceuticals v H N Norton & Co [1996] RPC 76

Is there a process or product identical to yours (prior state of art)?*	Yes	No
Has the invention been used in public so its operation made is known?	Yes	No
Have the details of the invention publicly disseminated?**	Yes	No

**For answering this question, one has to perform an online search, using the invention/creation keywords, in the following browsers/databases:*

European Patent Office (EPO) *Spanish Patent & Trademark Office (OEPM)*

United States Patent and Trademark Office (USPTO) *Japan Patent Office (JPO)*

PubMed Database *SCOPUS Database*

An invention shall be taken to be new if it does not form part of the state of the art.

The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else) which has at any time before the priority date of that invention been made available to the public (whether in the country where the invention would be patented or elsewhere) by written or oral description, by use or in any other way.

***The discussion of the details related to the invention with fellow researchers, partners and advisors is considered as confidential. It is highly recommended to sign confidential agreements.*

- **Inventive Step, Non-Obvious (A). Values: 1-10.**

The inventive step (**A**) may be any value between 1 and 10. This test has an initial value of 1 and 3 points for each of the options/answers bold marked can be added up a total **A** value of 10.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Genentech Inc.'s Patent, [1989] R.P.C. 147 (C.A.)
Biogen Inc. v. Medeva Plc [1997] R.P.C. 1

If the invention/creation is the combination of several ones, are their properties or functionality predictable if you know all its components? *	Yes	**No**
If the invention/process is the solution to a problem, are there different solutions possible so the inventor had to research and select the best one?**	**Yes**	No
Is the invention the replacement of one of the components of the product/process for a different one with equivalent properties?	Yes	**No**

**If the properties are greater than the sum of its parts, or better than expected, then it can be considered as a non-obvious invention. And then, the answer to the previous question should be "No".*

Summing up: patentability requires that several features are met (including: surprising technical advantages, unexpected technical effects). Mere aggregations (developments in one way street -lack of alternatives) are not patentable.

***If there is only one solution to a problem in a process, object or invention, and it could be deduced by a person skilled in the art, it might be considered obvious.*

- **Industrial Application, Capable of Industrial Application, Useful (I). Values: 1-10**

This test has an initial value of 1, to which are added 3 points for each of the options/answers bold marked.

For clarifying the questions of this part of the questionnaire, it is advisable to read the following article/case:
Eli Lilly v Human Genome Sciences [2010] EWCA Civ 33, overruled [2011] UKSC 51

Is the industrial field totally clear in the invention description?*	**Yes**	No
Is the main application of the invention related to the private and personal sphere of human being?	Yes	**No**
Is the invention described clear and complete enough for being carried out by a person skilled in the art?**	**Yes**	No
Is the invention a method for treatment of the human or animal by surgery or therapy or a diagnostic method practiced on the human or animal body?***	Yes	**No**

**It must be specified the industry the invention is addressed to (the term "Industry" is far-reading). It is especially important when the invention refers to DNA sequences.*

An invention shall be taken to be capable of industrial application if it can be made or used in any kind of industry, including agriculture.

***Requirement of sufficiency of disclosure.*

Disclosure*: the matter relied upon as prior art must disclose subject matter that, if performed, would necessarily result in an infringement of the patent.*

*******Eliminatory question****. If the answer to this question is "Yes" the P.I. automatically becomes "0". This restriction does not apply to an invention consisting of a substance or composition for use in any such method.*

D. iGEM VALENCIA BIOCAMPUS SURVEY ON IP

We conducted a survey in order to find out what is the opinion of the society on our patentability formula and our idea of improving the IP framework. Thus, we carried out an online survey – in English and Spanish- focusing on specific groups. These groups are iGEM participants, lawyers, biotechnologists, general public and engineers.

The survey consisted of just a simple question about whether patentability of a technical invention should be decided by the person skilled in the art or it would be better to use a formula. We proposed three options to choose among them:

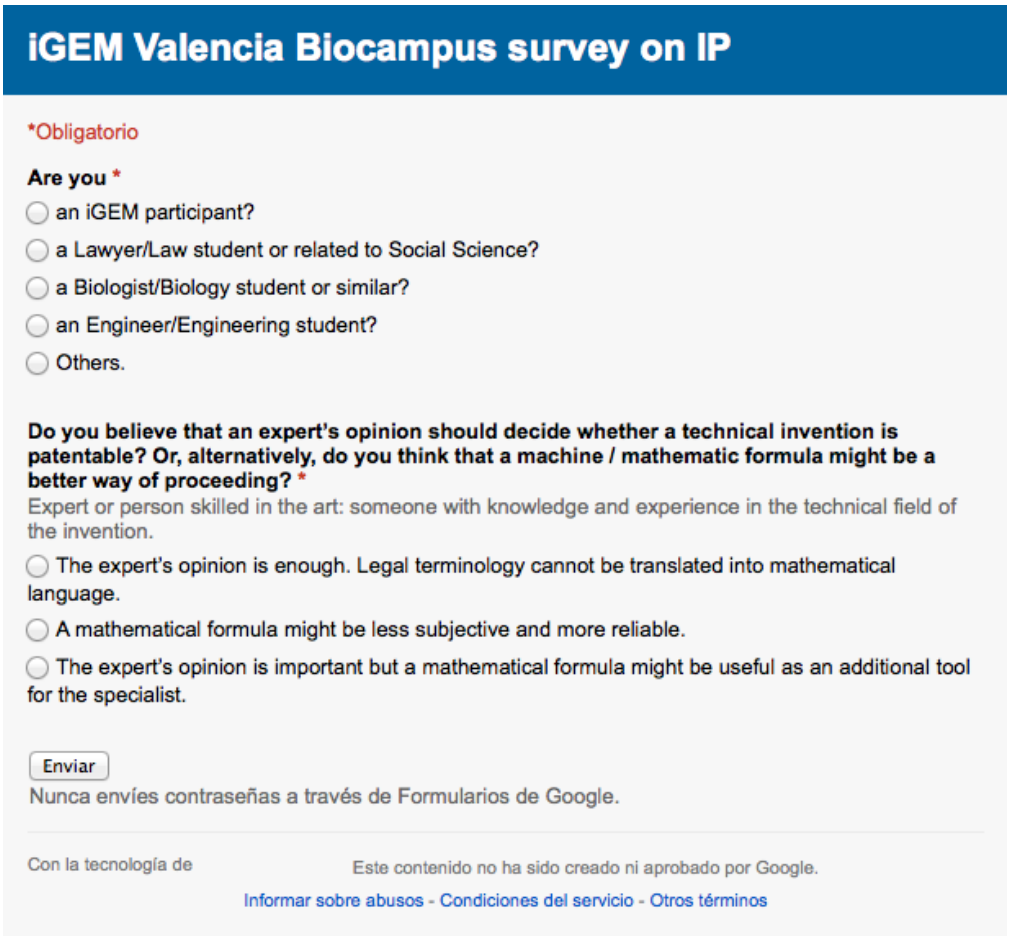

Figure 4. English version of our online survey.

Results of the survey

After two and a half months of the survey start, the results are summarized on the pie charts shown below. The final number of participants was 526. Each group was well-represented (14-26%) and although slight differences among groups are detectable (lawyers were less prone to use maths) a vast majority of respondents (70-83%) found using maths in IP a helpful possibility.

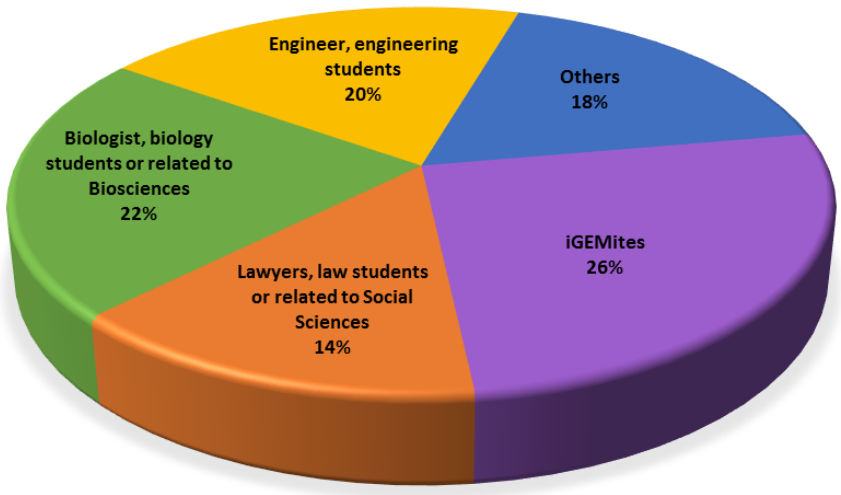

Figure 5. Percentage of participation –by background- in the survey. iGEMites are the majoritarian group with a 26% of participation, in a second place (22%) are the biologists -or related to the field- followed by the engineers or similar (20%). The lowest participation rate is for the lawyers or related to social sciences (only 14% of the responses came from this group).

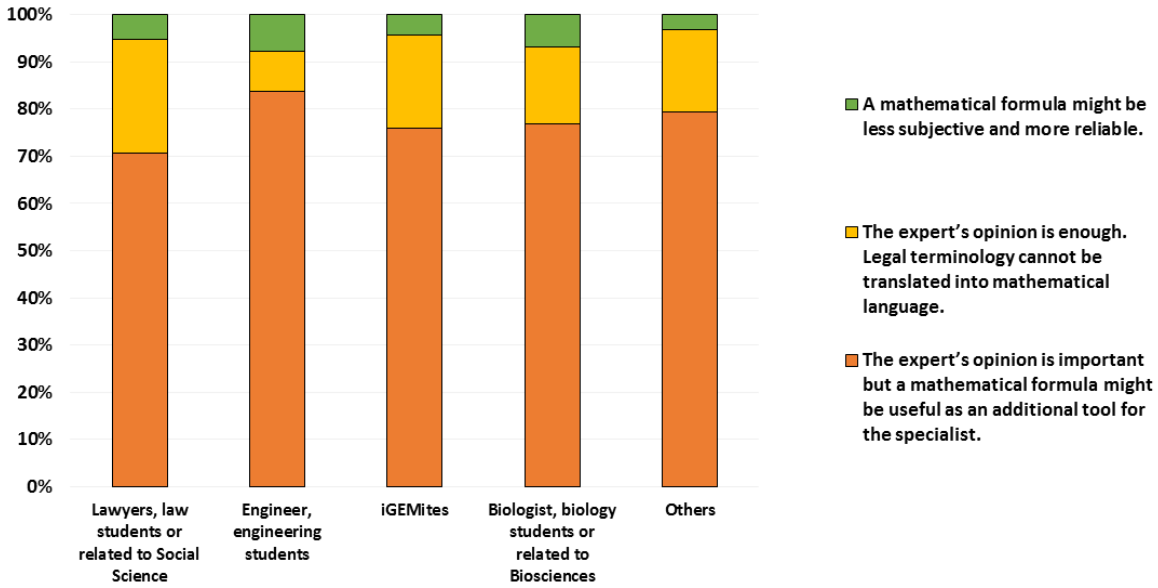

Figure 6. Results of our survey shown in percentage and grouped by field of knowledge. As it can be observed, the favourite option in all the groups was the third one: *The expert's opinion is important but a mathematical formula might be useful as an additional tool for the specialists*. However, differences among the different backgrounds exist being specially pronounced between the group of engineers and lawyers.

E. ANNEX I BIBLIOGRAPHY AND REFERENCES

Article 52. European Patent Convention (EPC).

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Section 5.Patents. Part II TRIPS Agreements.

Chapter I and II. Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.

Association for Molecular Pathology et al. v. Myriad Genetics (USA).

ANNEX II.
BRIEF DICTIONARY OF IP AND SB TERMS

TERMS FOR SCIENTISTS-ENGINEERS AND LAWYERS, RESPECTIVELY

DICTIONARY FOR BIOLOGISTS[17]

- **Appeal**: to challenge a decision taken by a Patent Office, such as a decision to refuse to protect the technology or the invention subject of a patent application.
- **Applicant**: natural person or legal person applying for the granting of an Industrial Property Right (e.g., patents or trademarks).
- **Application** (of an Industrial Property Right): a request filed by an Applicant or by the Applicant's agent on its behalf for the granting of an Industrial Property Right.
- **Availability to the Public**: to give to the public the information of the registered invention.
- **Board of Appeal**: Body responsible for examining appeals against decisions taken by the relevant Patent Office.
- **Claims**: the main part of a patent document which defines the scope of the technology/invention's protection. Also, it could refer to a lawsuit against counterparties.
- **Classification**: in patents, it means a specific system which subdivides the relevant technology into different subcategories. Each subcategory classifies a patented invention depending on its technical characteristics. It also applies for other industrial property rights like trademarks.
- **Description of the Invention/Technology**: it is one of the essential parts of patent documents that helps the claims to define the scope of protection. It includes a summary of the invention, its technical field, the technology's background and the essential features of the invention with reference to relevant drawings.
- **Disclosure**: to reveal to the public the contents of an invention claimed. To be valid for purposes requesting protection under a patent law, such a disclosure must be made in a manner sufficiently clear and complete for the invention to be carried out by a person knowledgeable in the field.
- **EPO**: European Patent Convention is a legal instrument that provides a legal framework for the granting of European patents before the European Patent Office. It provides a unique set of rules to harmonise procedures between European states in order to avoid filing separate patent application in each country with different requirements.
- **Examination**: related to patents means to see whether the application complies with the patentability or registrability requirements of the

[17] *GLOSSARY OF TERMS CONCERNING INDUSTRIAL PROPERTY INFORMATION AND DOCUMENTATION*. HANDBOOK ON INDUSTRIAL PROPERTY INFORMATION AND DOCUMENTATION. WIPO (June 2013)

industrial property law. The examiner who is an industrial property law authority performs this job.

- **File**: it means the totality of documents pertaining to a given patent application or granted patent.
- **Industrial Design**: it is a type of industrial property protection which protects the visual aspect of an object, including its two-dimensional and three-dimensional features of shape and surface.
- **Industrial Property**: type of intellectual property that protects industrial application inventions granting rights such as patents, trademarks, designs, mask works and plant breeders.
- **Infringement**: violation of an exclusive industrial property right by selling or using a patented product or process without the permission of the right's owner.
- **Intellectual Property**: creation of the mind. It is divided into two categories: (i) industrial property, which includes patents, trademarks, industrial designs, and (ii) copyright, which includes literary and artistic works such as novels, poems and plays, films, musical works, artistic works such as drawings, paintings, photographs and sculptures, and architectural designs, amongst others.
- **Invention**: new product, process or machinery or any new use thereof. It must fulfil some essential requirements to be patentable.
- **Inventor's Certificate**: a document similar to an invention disclosure form that exists in several countries, which function is to acknowledge the authorship of an invention to its inventor(s), disregarding patents.
- **Inventive Step**: one of the requirements that an invention must match in order to be patentable. It means that considering the invention's state of the art, the invention is not obvious (see Obviousness) to a person skilled in the art.
- **Know-how**: it is a transferable right which consists on the knowledge of a particular person regarding non disclosed and valuable industrial information that can be of economic, financial, technical and/or organizational nature. It is limited accessible, usable and exploitable and is deemed to have protection until it becomes part of the public domain.
- **Licensing**: consists on granting the right to exploit a patent application or a patent by the licensor to a licensee.
- **Litigation**: an action brought in court to enforce a particular right.
- **Morality**: related to the belief that some behaviour was right and acceptable whereas other behaviour was wrong, this belief being founded on the totality of the accepted norms which were deeply rooted in a particular culture. For the purposes of the EPC, the culture in question was the culture inherent in European society and civilisation. Accordingly, inventions the exploitation of which was not in conformity with the conventionally accepted standards of conduct pertaining to this culture were to be excluded from patentability as being contrary to morality.
- **Novelty**: a condition for patentability in all the jurisdictions. An invention is new if it does not form part of the State of the Art, that is, the invention was not available to the public, in any form, before the filing of the patent application.
- **Obviousness**: a characteristic of an invention which means that if a person with ordinary skill in the relevant field of technology can deduce it from publicly available information (prior art), then it does not meet the conditions for patentability.
- **Official Gazette**: official bulleting or journal published by Patent Offices, which records information on the procedural steps taken in respect

of concrete industrial property rights, as well as on official communications of the office, the changes of the current industrial property laws, or the legal status of patent documents, etc. They usually give information regarding at the status of a concrete invention.

- **Order public**: Protection of public security and the physical integrity of individuals as part of society. It also encompassed the protection of the environment. Accordingly, inventions the exploitation of which was likely to seriously prejudice the environment were to be excluded from patentability as being contrary to "ordre public". **Paris Convention**: is the basic international convention held in Paris in 1883 in the field of industrial property, adhered by over 100 States. Its aim is to warrant the same kind of protection for all the contracting States.
- **Patent**: it is a title of legal protection of an invention issued, upon application and subject to meeting legal criteria, by a government office. The rights conferred by a patent are the rights to prevent others from making, using, selling, offering for sale or importing a product, a process, or a product obtained by a (patented) process.
- **Patent Family**: it is the collection of different patent documents relating to the same invention or several inventions sharing a common aspect that are published at different times in the same country or published in different countries or regions.
- **Patentee**: the owner of the patent, who has the right to exploit it, directly or indirectly, through others.
- **Person skilled in the art**: Someone with knowledge and experience in the technical field of the invention. He or she is a fiction person who serves as a reference to examine if the invention is patentable or not according to its knowledge and experience.
- **Plant Breeder's Rights**: it offers legal protection to "breeders" or plant producers of new varieties of plants.
- **Priority Application**: Article 4 of the Paris Convention allows to apply for a "priority" patent in a particular territory and then to file a foreign patent application in other territories claiming the same date as the one given for the priority patent within 1 year from the priority application.
- **Publication**: in patents, it means making available the contents of a document to the public, usually at the Official Gazette.
- **TRIPS Agreement**: the most important multilateral agreement on intellectual property rights. It set down minimum standards that covers copyrights; trademarks; geographical indications; industrial designs; patents including the protection of new varieties of plants; layout-designs of integrate circuits; and undisclosed information including trade secrets and test data. The three main characteristics of this agreement are standards, enforcement and dispute settlement.
- **Refusal**: Decision of not granting a patent application because it does not fulfil the necessary / essential requirements.
- **Register** (of Industrial Property Rights): Register kept by an industrial property office in which is recorded the legal status of different industrial property rights. Usually, the office keeps separately a patent register, a trademark register and an industrial design register.
- **State of the Art**: it means the knowledge of a particular technical field available or disclosed to the public in a particular period of time, in a particular territory.
- **Term**: Maximum period for which a patent can be legally valid.

- **Trade Mark**: also known as mark. It is a sign that serves to identify the goods and the services of an industrial or a commercial enterprise or a group of such enterprises from the goods and the services of others persons. It may consist on a character, a drawing, colours or combination of them.
- **Utility Model**: a right addressed to protect minor inventions upon application, in accordance with requirements somewhat less strict than those for obtaining patent protection and to a lesser extent. The rights conferred by this title are similar to the patent rights.
- **WIPO** (World Intellectual Property Organization): Specialized agency of the United Nations (UN), which aims are to protect and grant cooperation upon intellectual property rights. It provides a global policy forum where governments, intergovernmental organizations, industry groups and civil society come together to address developing IP issues.

- **Antibiotic**: an antibiotic or antimicrobial is a compound or molecule that kills (**microbicide/microbiolitic**) or inhibits the growth of the microorganism (**microbiostatic**).
- **Antibiotic resistance**: some microorganisms have either mechanisms that allow them overcoming this selective agents or structures (antibiotic targets) insensitive to them. Those microbes are then naturally resistant to certain antibiotics so they can grow in the presence of those agents. Others, by contrast, are sensitive but can become resistant through acquisition of sequences of DNA (**genes of resistance**). This strategy is widely used in molecular biology to select cells with characteristics of interest (like a **BioBrick**).
- **Asepsis**: working procedures that avoid the surrounding environmental microorganisms to enter the working area.
- **Antisepsis**: methods or procedures that prevent the development of microorganisms, being able to even kill them (antiseptic refers to compounds used only on the surface of the body).
- **Viable non-cultivable cells**: under certain non-favourable conditions (strong stresses, for example) some cells come into this state where they are not able to be cultured in the conventional media but present an active metabolism.
- **BioBrick**: DNA sequence that presents, at the ends, known restriction sites (**prefix** and **suffix**) that allow using **BioBricks** as standard interchangeable parts (you can cut and paste them into the vector of your choice, as a Lego piece) with a view to build engineering biological systems.
- **Biotechnology**: science that uses organisms or their metabolic products to get either a development, a tool or a procedure of interest (research, medical applications, industry…).
- **Biological chassis**: a structure that supports a man-made object. In the frame of **Synthetic Biology**, a biological chassis would be understood as the biological system (bacteria, yeast…) that supports the man-made object, i.e. the **BioBrick**.
- **Clone** (verb): process of cutting, purifying and pasting fragments of DNA (such as **BioBricks**) from one vector to another (among plasmids, for example) and amplifying them in the vectors upon transfer in (typically) bacteria or yeast.
- **Competent cell**: cell (typically bacteria or yeast) that is able to take up foreign DNA (from outside the cell). This transformation process, essential in molecular biology, allows to introduce fragments of DNA of interest (genes, promoters…) into a biological chassis. Here, it is necessary to differentiate between two concepts: natural/induced competency and **chemiocompetent/electrocompetent** cells. There are three main ways to transform a cell or, in other words, to introduce DNA into it:
  - **Transformation**: the DNA is taken up from the environment as explained above.
  - **Conjugation**: here there are two cells, a donor and an acceptor one. The donor has a plasmid with the information for sexual pili synthesis, a bridge that allows the movement of DNA among the two bacteria.
  - **Transfection**: viruses act like vectors. A cell is infected by a virus and in the process some fragments of DNA are introduced into the bacteria chromosome.
- **Electrophoresis**: technique where DNA is forced to move thought a network (tangle like) following an

electric field. As the DNA is negatively charged it will move from the negative pole to the positive one in such a way that the DNA molecules will be separated by their size (the molecules have to move into the network). DNA fragments can be visualized because of an added agent that inserts itself into the DNA molecule and fluoresces under ultraviolet light. An example of this method would be as follows: we have a **BioBrick** (insert) we want to release from an "origin plasmid", purify and clone into a "destination plasmid" (the plasmids and the **BioBrick** have different sizes); so, after digesting we carry out an electrophoresis for purifying the band corresponding to the **BioBrick**, now we ligate and transform. We select some colonies from transformants obtained, carry out a **miniprep** followed by a digestion and we check if the sizes observed in the electrophoresis gel are the expected ones: **BioBrick** & destination plasmid.

- **Genetic Engineering**: set of techniques for DNA incorporation to an organism to become a Genetically Modified Organism or GMO. The origin of this DNA can be an organism from the same species (**cisgenesis**) or from a different one (**trangenesis**).
- **Genotype**: set of genes from an organism. Based on the information obtained from the genotype the organism potential can be determined (what the organism could be).
- **Glycerinate**: method for microorganisms storage based on cryopreservation using glycerol as protecting agent (when water solidifies it forms crystals that can break the cells, by adding glycerol the damage is reduced due to the limited number of water crystals formed).
- **Medium**: set of nutrients (carbon, nitrogen, sulphur…) needed for the correct development, growth and division of cells (bacteria, yeast, human cells…). The media can be liquid or solid (agar added). It can be also supplemented for specific microbial requirements (a specific compound can be required for a particular microorganism) or for selecting some interesting characteristics.
- **Microbial Culture**: methodology used for microbial growth (cell multiplication in a culture medium) under controlled lab conditions.
- **Miniprep**: technique for plasmid extraction in small (typically several micrograms) scale.
- **Model organism**: organism that due to its short generation time, accessibility for working with (one could hardly work with a group of elephants in a molecular biology laboratory, for example), and well characterized genome and biology is used for the study and characterization of different biological phenomena (disease, traits…). Some model organisms are: the fly *Drosophila melanogaster*, the worm *Caenorhabditis elegans*, the toad *Xenopus laevis*, the baker's yeast *Saccharomyces cerevisiae* and the bacterium *Escherichia coli*, among others.
- **Modelling**: mathematical description of a biological system.
- **Phenotype**: observable characteristics of an organism (eye colour, for example). The phenotype of an organism is the result of the genetic background of the organism (the **genotype**) and the environmental conditions.
- **Plasmid**: circular DNA molecule. This molecule is separated and replicates independently of the chromosome (autonomous regulation). The most remarkable parts in a plasmid are: the **multicloning site** (plasmid region where a high number of restriction sequences can be found, in such a way that it makes possible to clone DNA fragments with different ends), the **replication origin** (dictates the

number of plasmid copies in the cell; based on this, the plasmids can be classified as high, medium and low copy number) and the **resistance cassette** (it makes possible the selection of cells transformed with the plasmid). There are two main kinds of plasmids according to the objective: **expression plasmids** (these plasmids are designed for the expression of cloned sequences) and **cloning plasmids** (these plasmids allow the amplification and maintenance of a sequence of interest).

- **Promoter**: DNA sequences where the transcription (first step of a gene expression) of a gene is started. The promoter also dictates when, under which conditions, genes are expressed (stress, in the presence of "x" molecules, constitutively, etc).
- **Protein**: biological molecules whose basic units are the amino acids. The proteins perform an array of functions in living organisms. From this group, the **enzymes** (proteins that catalyse biochemical reactions in the cell) stand out, since lot of them are widely used in molecular biology. Some examples of these enzymes are the **ligase** (enzyme that catalyses the joining of two DNA molecules), the **polymerase** (enzyme able to synthetize DNA from its basic elements; used in the DNA copy process called PCR) and the **restriction enzymes** (enzymes capable of break DNA at specific sequences, generating specific ends that will make possible the later joining with other molecule with equal ends).
- **Reporter gene**: gene whose output is easily measurable (fluorescence, for example).
- **Sterility**: process in which all the forms of life are killed, even the bacterial spores (the most resistant forms of life known).
- **Synthetic Biology**: interdisciplinary discipline whose goal is the construction and design of biological devices and systems through the application of the engineering principles to the field of biology.
- **Terminator**: DNA sequence that marks the end of a concrete gene.
- **Vector**: vehicle used to transfer genetic material, DNA, to a cell. A vector described previously would be a **plasmid**, for example.